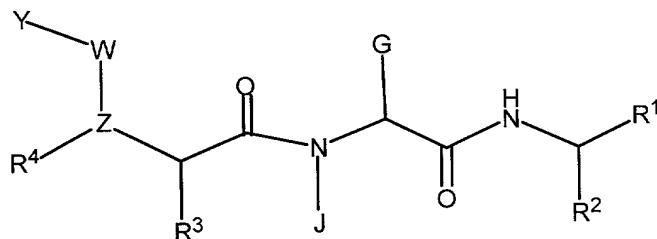


Claims

What is claimed is:

1. A compound, including enantiomers, stereoisomers, rotamers and tautomers of said compound, and pharmaceutically acceptable salts or solvates of said compound, said compound having the general structure shown in Formula I:



10

Formula I

wherein:

G, J and Y may be the same or different and are independently selected from the group consisting of the moieties: H, alkyl, alkyl-aryl, heteroalkyl, heteroaryl, aryl-heteroaryl, alkyl-heteroaryl, cycloalkyl, alkyloxy, alkyl-aryloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, cycloalkyloxy, alkylamino, arylamino, alkyl-aryl-amino, arylamino, heteroaryl-amino, cycloalkylamino and heterocycloalkylamino, with the proviso that Y maybe additionally optionally substituted with X¹¹ or X¹²;

X¹¹ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkyl-alkyl, heterocyclyl, heterocyclalkyl, aryl, alkylaryl, arylalkyl, heteroaryl, alkylheteroaryl, or heteroarylalkyl moiety, with the proviso that X¹¹ may be additionally optionally substituted with X¹²;

X¹² is hydroxy, alkoxy, aryloxy, thio, alkylthio, arylthio, amino, alkylamino, arylamino, alkylsulfonyl, arylsulfonyl, alkylsulfonamido, arylsulfonamido, carboxy, carbalkoxy, carboxamido, alkoxycarbonylamino, alkoxycarbonyloxy, alkylureido, arylureido, halogen, cyano, or nitro, with the

proviso that said alkyl, alkoxy, and aryl may be additionally optionally substituted with moieties independently selected from X¹²;

R¹ is COR⁵ or B(OR)₂, wherein R⁵ is selected from the group consisting of H, OH, OR⁸, NR⁹R¹⁰, CF₃, C₂F₅, C₃F₇, CF₂R⁶, R⁶ and
 5 COR⁷ wherein R⁷ is selected from the group consisting of H, OH, OR⁸,
 CHR⁹R¹⁰, and NR⁹R¹⁰, wherein R⁶, R⁸, R⁹ and R¹⁰ may be the same or different and are independently selected from the group consisting of H, alkyl, aryl, heteroalkyl, heteroaryl, cycloalkyl, cycloalkyl, arylalkyl, heteroarylalkyl,
 CH(R^{1'})COOR¹¹, CH(R^{1'})CONR¹²R¹³, CH(R^{1'})CONHCH(R^{2'})COO R¹¹,
 10 CH(R^{1'})CONHCH(R^{2'})CONR¹²R¹³, CH(R^{1'})CONHCH(R^{2'})R',
 CH(R^{1'})CONHCH(R^{2'})CONHCH(R^{3'})COO R¹¹,
 CH(R^{1'})CONHCH(R^{2'})CONHCH(R^{3'})CONR¹²R¹³,
 CH(R^{1'})CONHCH(R^{2'})CONHCH(R^{3'})CONHCH(R^{4'})COO R¹¹,
 CH(R^{1'})CONHCH(R^{2'})CONHCH(R^{3'})CONHCH(R^{4'})CONR¹²R¹³,
 15 CH(R^{1'})CONHCH(R^{2'})CONHCH(R^{3'})CONHCH(R^{4'})CONHCH(R^{5'})COO
 R¹¹, and
 CH(R^{1'})CONHCH(R^{2'})CONHCH(R^{3'})CONHCH(R^{4'})CONHCH(R^{5'}) CONR¹²R¹³,
 where R^{1'}, R^{2'}, R^{3'}, R^{4'}, R^{5'}, R¹¹, R¹², R¹³, and R' may be the same or different and are independently selected from a group consisting of H, alkyl,
 20 aryl, heteroalkyl, heteroaryl, cycloalkyl, alkyl-aryl, alkyl-heteroaryl, aryl-alkyl and heteroaralkyl;

Z is selected from O, N, or CH;

W maybe present or absent, and if W is present, W is selected from C=O, C=S, or SO₂; and

25 R, R', R², R³ and R⁴ are independently selected from the group consisting of H; C1-C10 alkyl; C2-C10 alkenyl; C3-C8 cycloalkyl; C3-C8 heterocycloalkyl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester,

carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro; oxygen, nitrogen, sulfur, or phosphorus atoms (with said oxygen, nitrogen, sulfur, or phosphorus atoms numbering zero to six); (cycloalkyl)alkyl and

(heterocycloalkyl)alkyl, wherein said cycloalkyl is made of three to eight

5 carbon atoms, and zero to six oxygen, nitrogen, sulfur, or phosphorus atoms, and said alkyl is of one to six carbon atoms; aryl; heteroaryl; alkyl-aryl; and alkyl-heteroaryl;

wherein said alkyl, heteroalkyl, alkenyl, heteroalkenyl, aryl, heteroaryl,

cycloalkyl and heterocycloalkyl moieties may be optionally substituted, with

10 said term "substituted" referring to optional and chemically-suitable substitution with one or more moieties selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, heterocyclic, halogen, hydroxy, thio, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, sulfonamide, sulfoxide, sulfone, sulfonylurea, hydrazide, and hydroxamate.

15 2. The compound of claim 1, wherein R¹ is COR⁵, and R⁵ is H, OH, COOR⁸ or CONR⁹R¹⁰.

20 3. The compound of claim 2, wherein R¹ is COCONR⁹R¹⁰, and R⁹ is H, R¹⁰ is selected from the group consisting of H, CH(R^{1'})COOR¹¹, CH(R^{1'})CONR¹²R¹³, CH(R^{1'})CONHCH(R^{2'})COOR¹¹, CH(R^{1'})CONHCH(R^{2'})CONR¹²R¹³, and CH(R^{1'})CONHCH(R^{2'})(R').

25 4. The compound of claim 3, wherein R¹⁰ is CH(R^{1'})CONHCH(R^{2'})COOR¹¹, CH(R^{1'})CONHCH(R^{2'})CONR¹²R¹³, or CH(R^{1'})CONHCH(R^{2'})(R'), wherein R^{1'} is H or alkyl, heteroalkyl and R^{2'} is phenyl, substituted phenyl, hetero atom-substituted phenyl, thiophenyl, cycloalkyl, piperidyl and pyridyl.

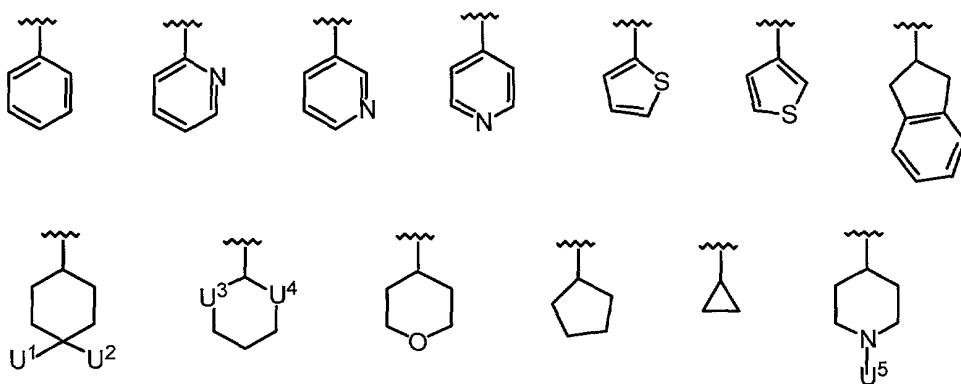
5. The compound of claim 4, wherein R^{1'} is H.

6. The compound of claim 5, wherein

R¹¹ is H or *tert*-butyl;

R' is hydroxymethyl; and

R^{2'} is selected from the group consisting of:



5

wherein:

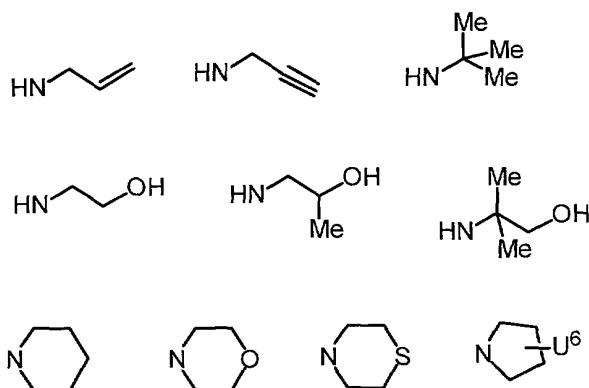
U¹ and U² maybe same or different and are independently selected from the group consisting of H, F, CH₂COOH, CH₂COOMe, CH₂CONH₂, CH₂CONHMe, CH₂CONMe₂, azido, amino, hydroxyl, substituted amino, substituted hydroxyl;

U³ and U⁴ maybe same or different and are O or S;

U⁵ is selected from the moieties consisting of alkylsulfonyl, aryl sulfonyl, heteroalkyl sulfonyl, heteroaryl sulfonyl, alkyl carbonyl, aryl carbonyl, heteroalkyl carbonyl, heteroaryl carbonyl, alkoxy carbonyl, aryloxy carbonyl, heteroaryloxy carbonyl, alkylaminocarbonyl, arylaminocarbonyl and heteroarylaminocarbonyl or combinations thereof; and

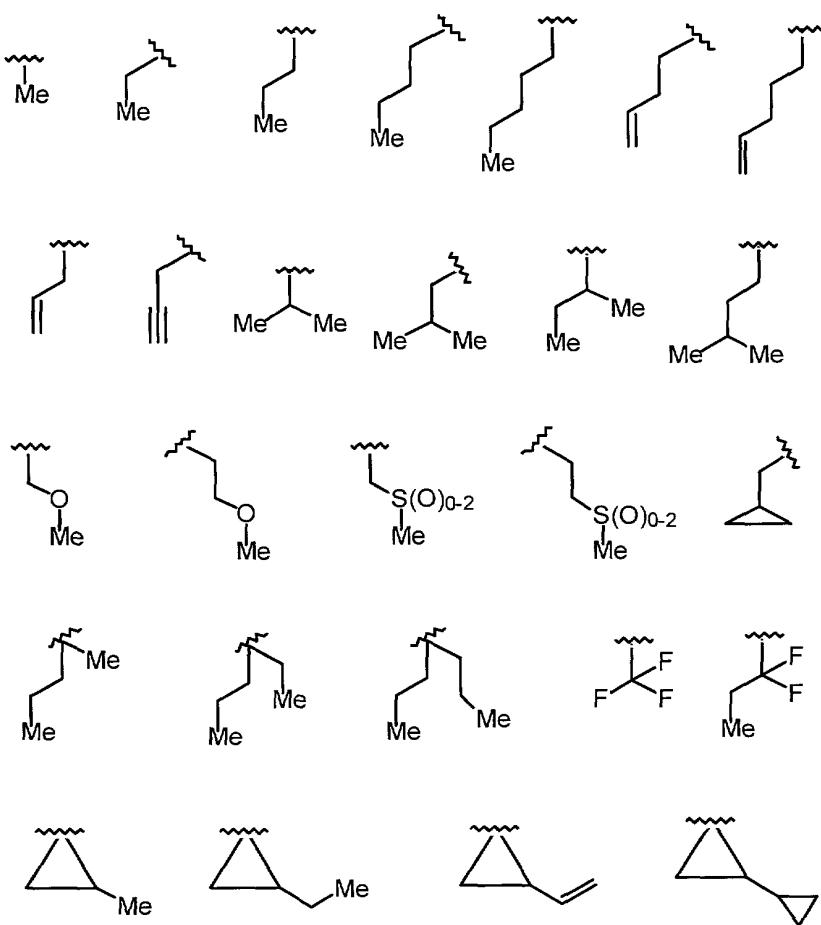
NR¹²R¹³ is selected from the group consisting of:

NH₂, NHMe, N(Me)OMe, NMe₂,

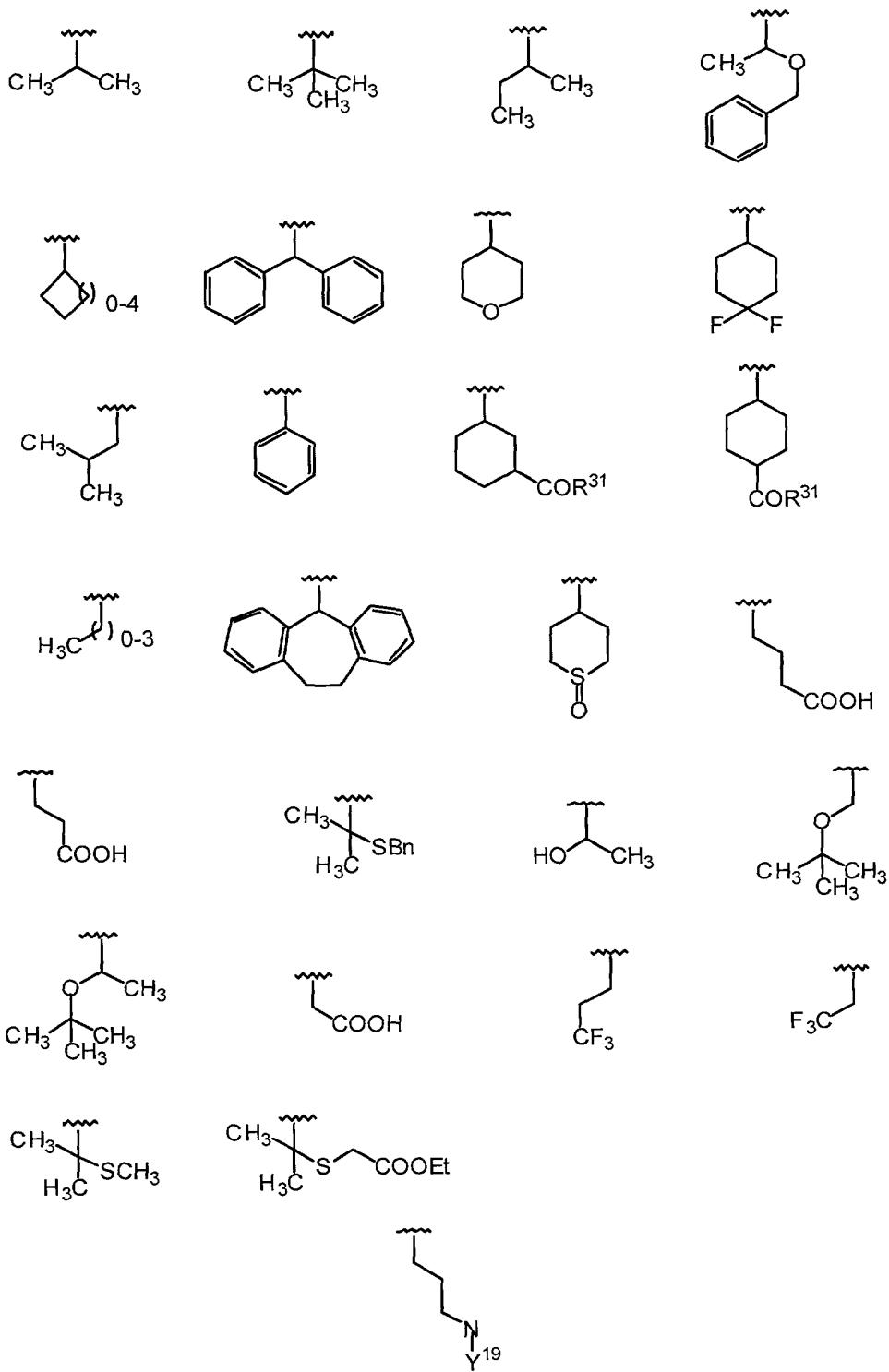


wherein U⁶ is H, OH, or CH₂OH.

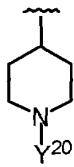
7. The compound of claim 2, wherein R² is selected from the group consisting of the following moieties:



8. The compound of claim 7, wherein R³ is selected from the group consisting of:

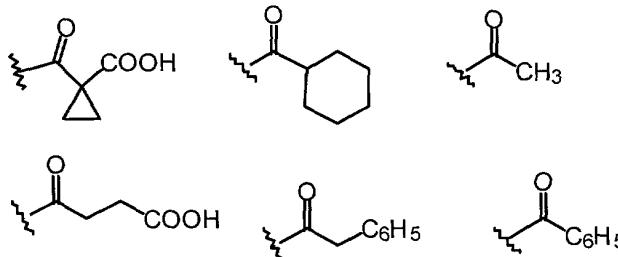


and



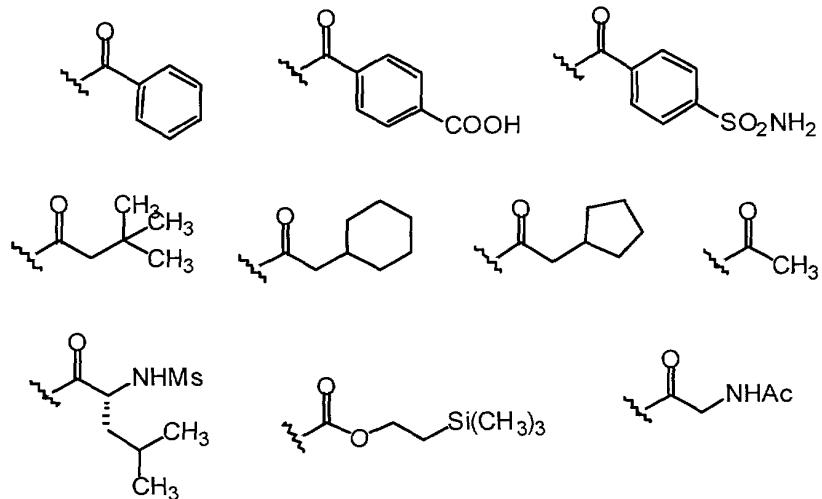
wherein $R^{31} = OH$ or O-alkyl;

Y^{19} is selected from the following moieties:

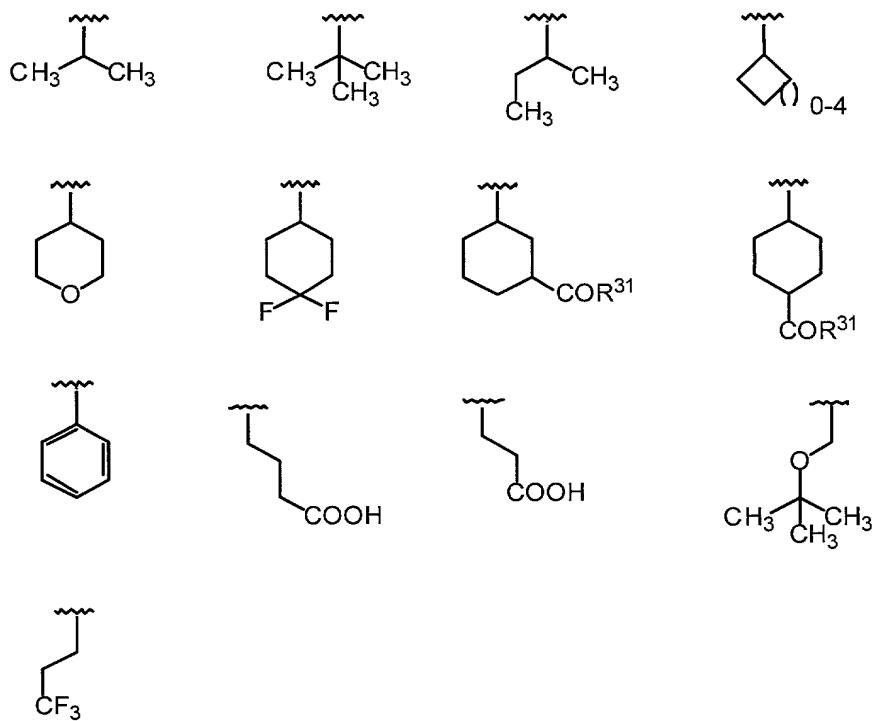


5

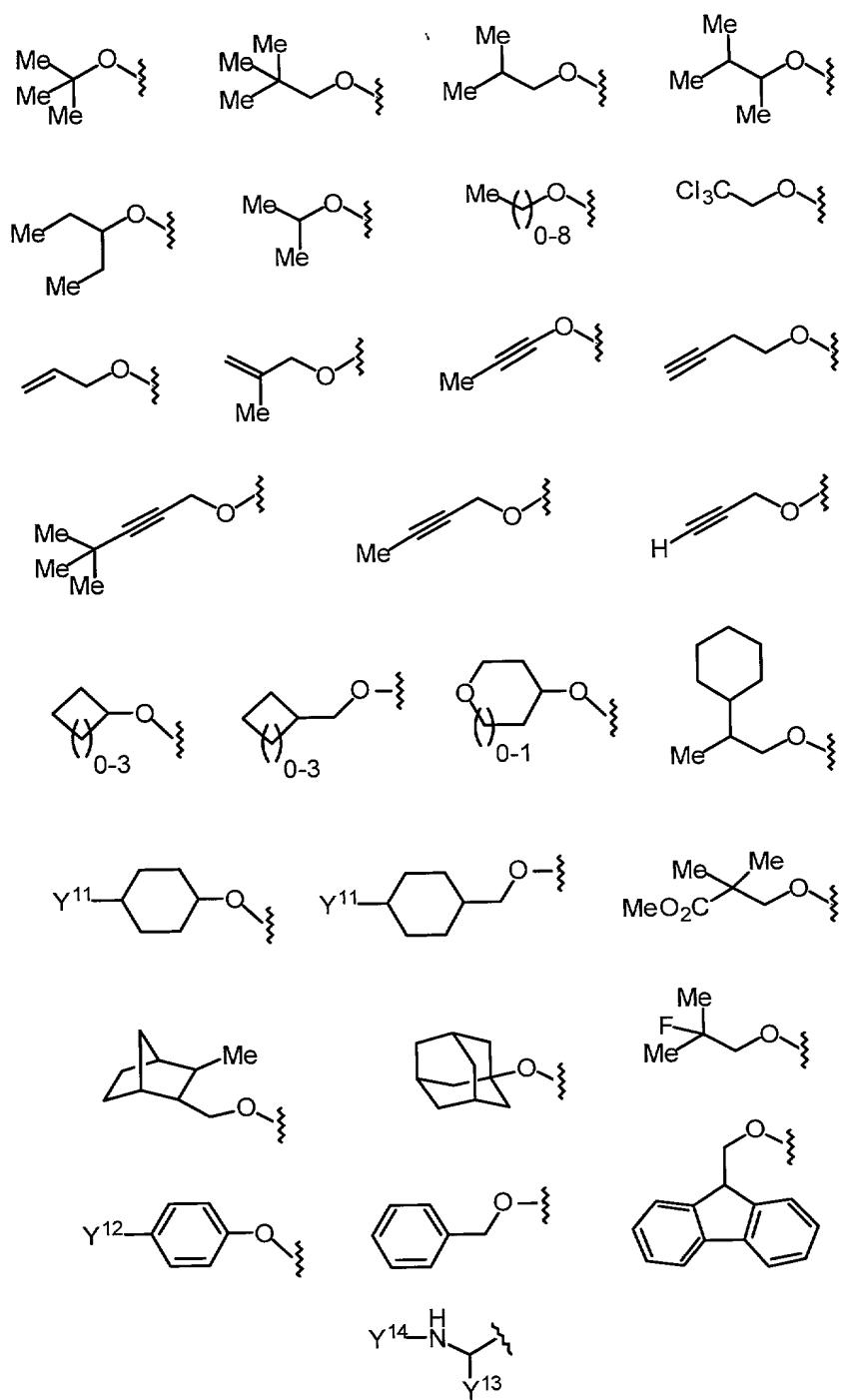
and Y^{20} is selected from the following moieties:

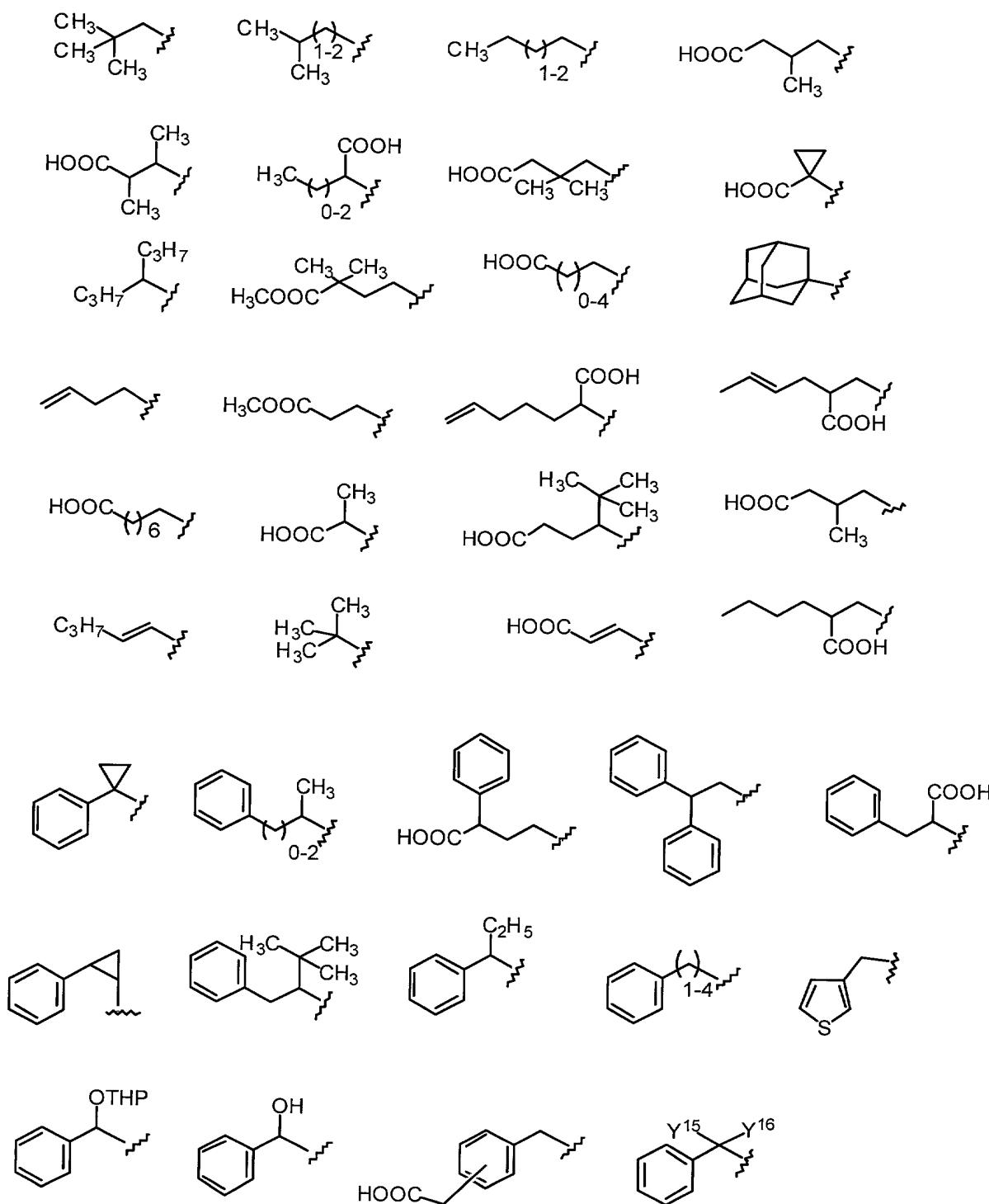


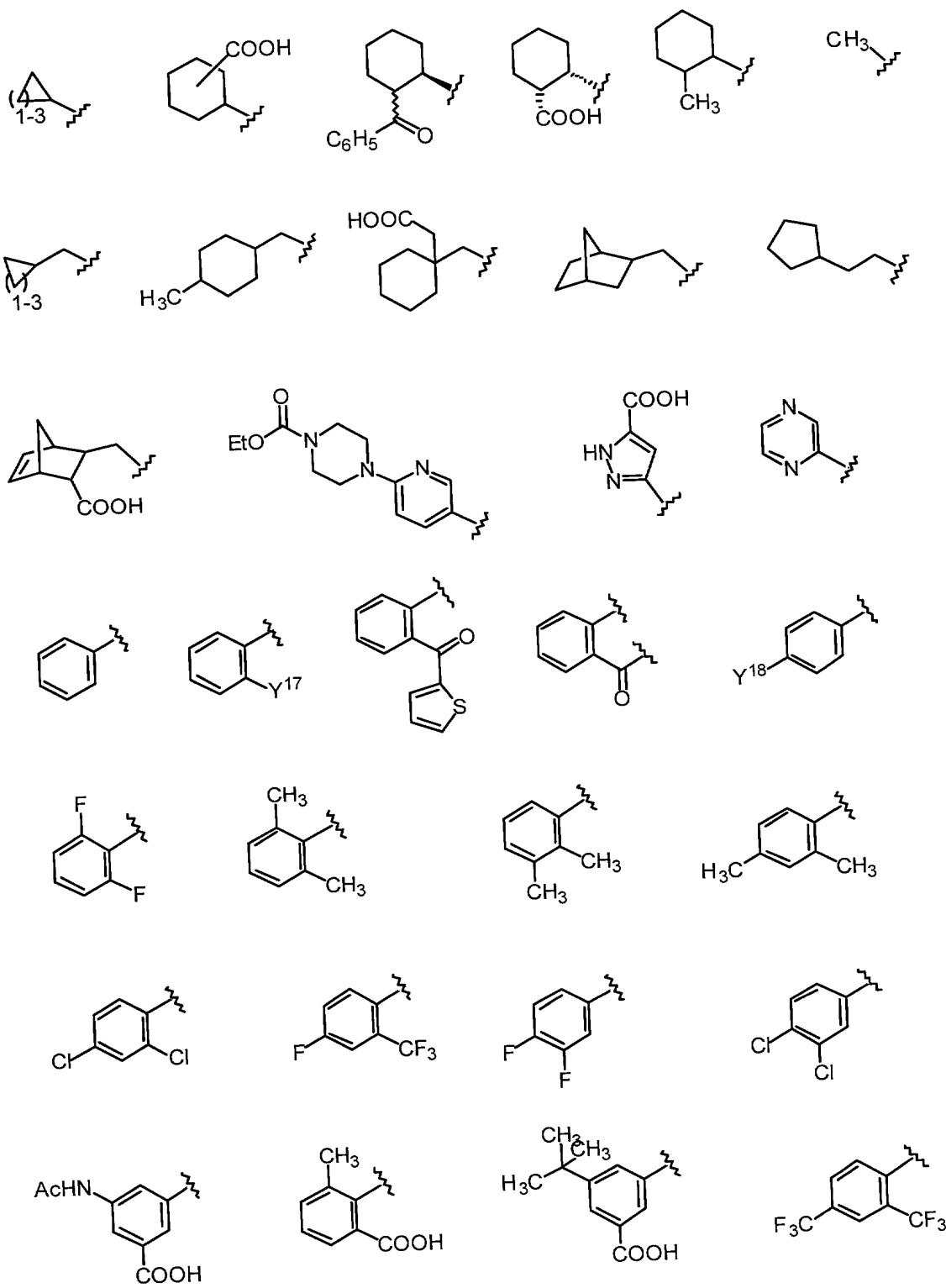
9. The compound of claim 8, wherein R^3 is selected from the following structures:

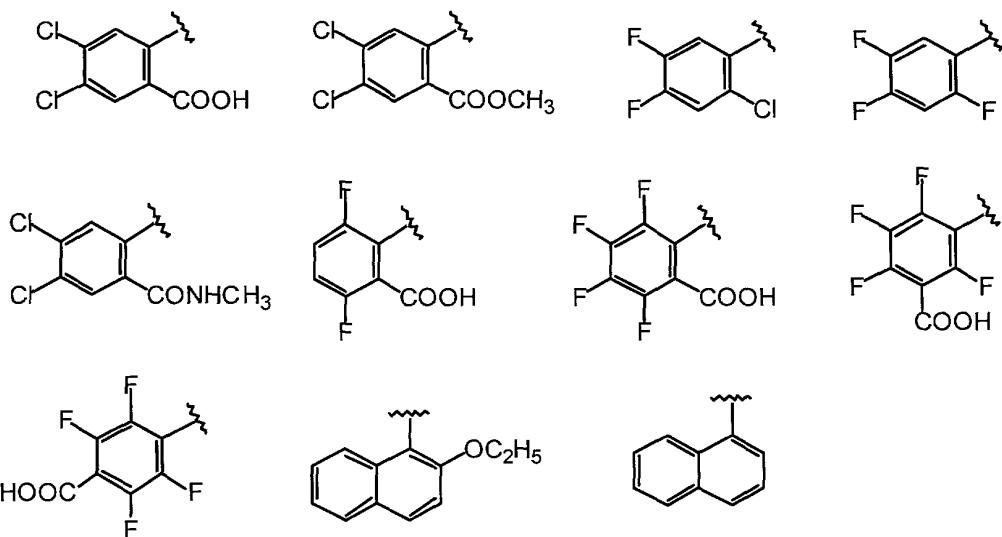


10. The compound of claim 9, wherein Z = N and R⁴ = H.
11. A compound of claim 10, wherein W is C=O, or SO₂.
12. A compound of claim 11, wherein Y is selected from the following
5 moieties:









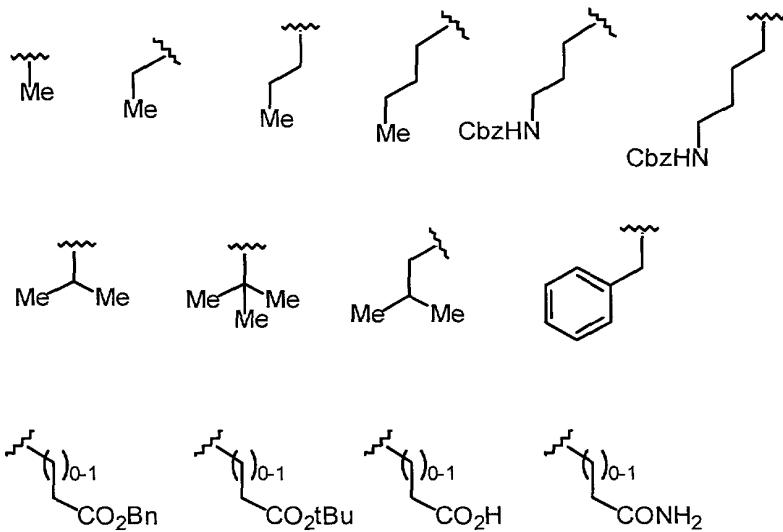
wherein:

5

Y^{11} is selected from H, COOH, COOEt, Ome, Ph, Oph, NHMe, NHAc, NHPh, CH(Me)₂, 1-triazolyl, 1-imidazolyl, and NHCH₂COOH;

Y^{12} is selected from H, COOH, COOMe, Ome, F, Cl, or Br;

Y^{13} is selected from the following moieties:



Y^{14} is selected from MeSO₂, Ac, Boc, iBoc, Cbz, or Alloc;

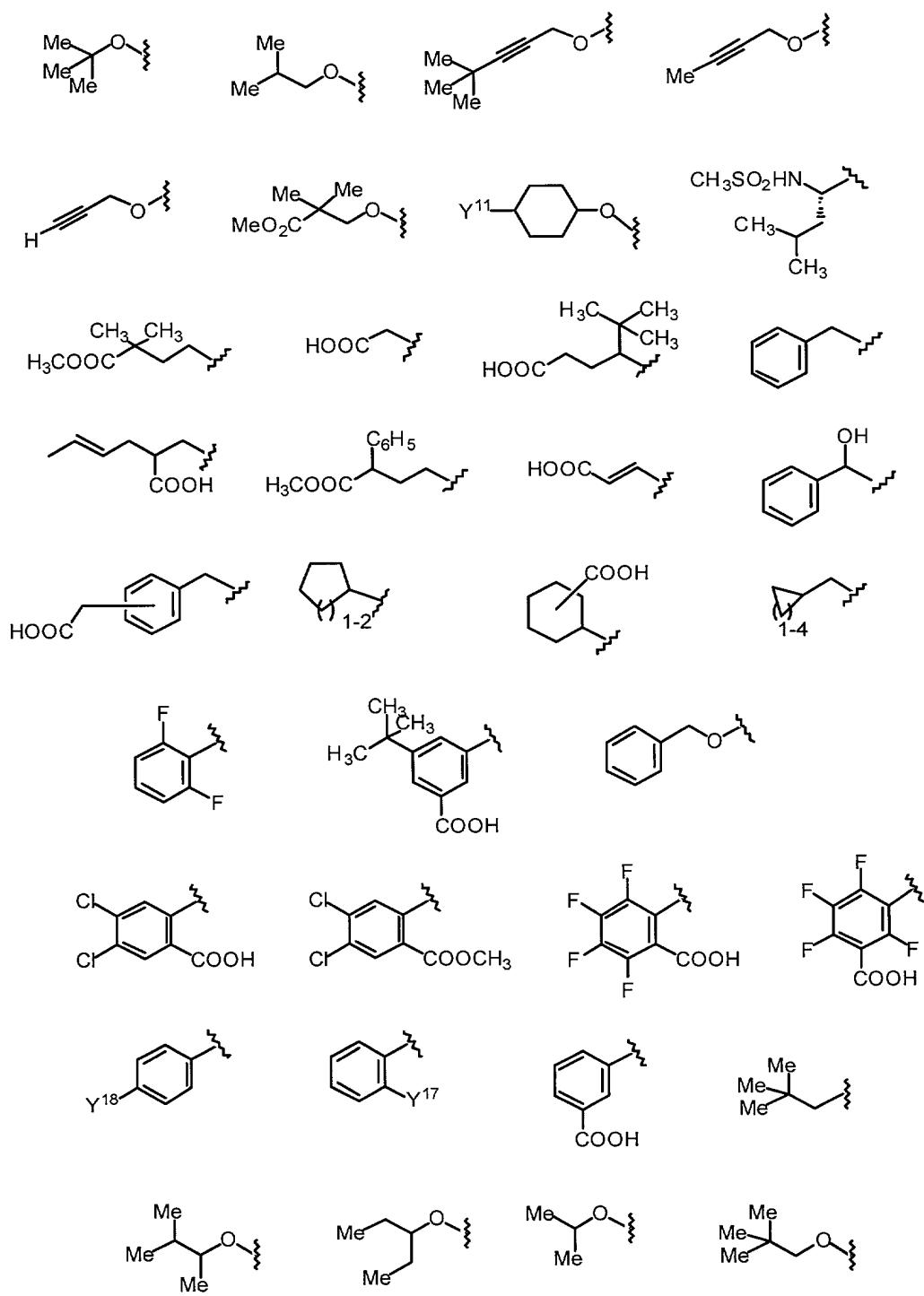
10

Y^{15} and Y^{16} may be the same or different and are independently selected from alkyl, aryl or heteroalkyl, or heteroaryl;

Y^{17} is CF₃, NO₂, CONH₂, OH, COOCH₃, OCH₃, OC₆H₅, C₆H₅, COC₆H₅, NH₂, or COOH; and

5 Y^{18} is COOCH₃, NO₂, N(CH₃)₂, F, OCH₃, CH₂COOH, COOH, SO₂NH₂, or NHCOCH₃.

13. A compound of claim 12, wherein Y is selected from the group consisting of:

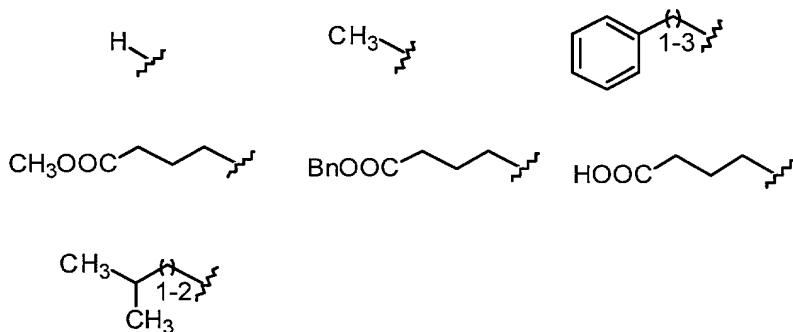


wherein:

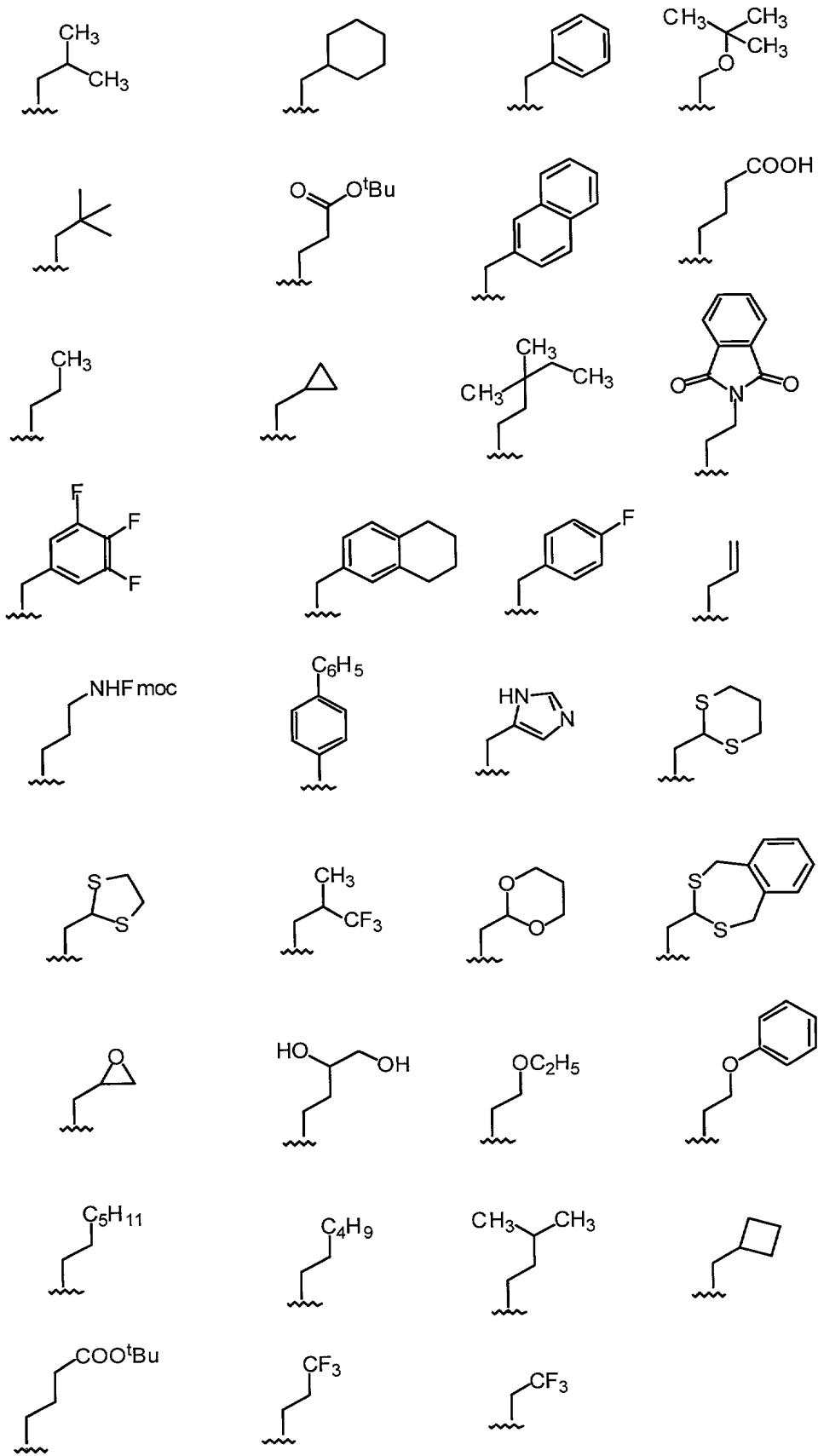
$Y^{17} = CF_3, NO_2, CONH_2, OH, NH_2$, or $COOH$;

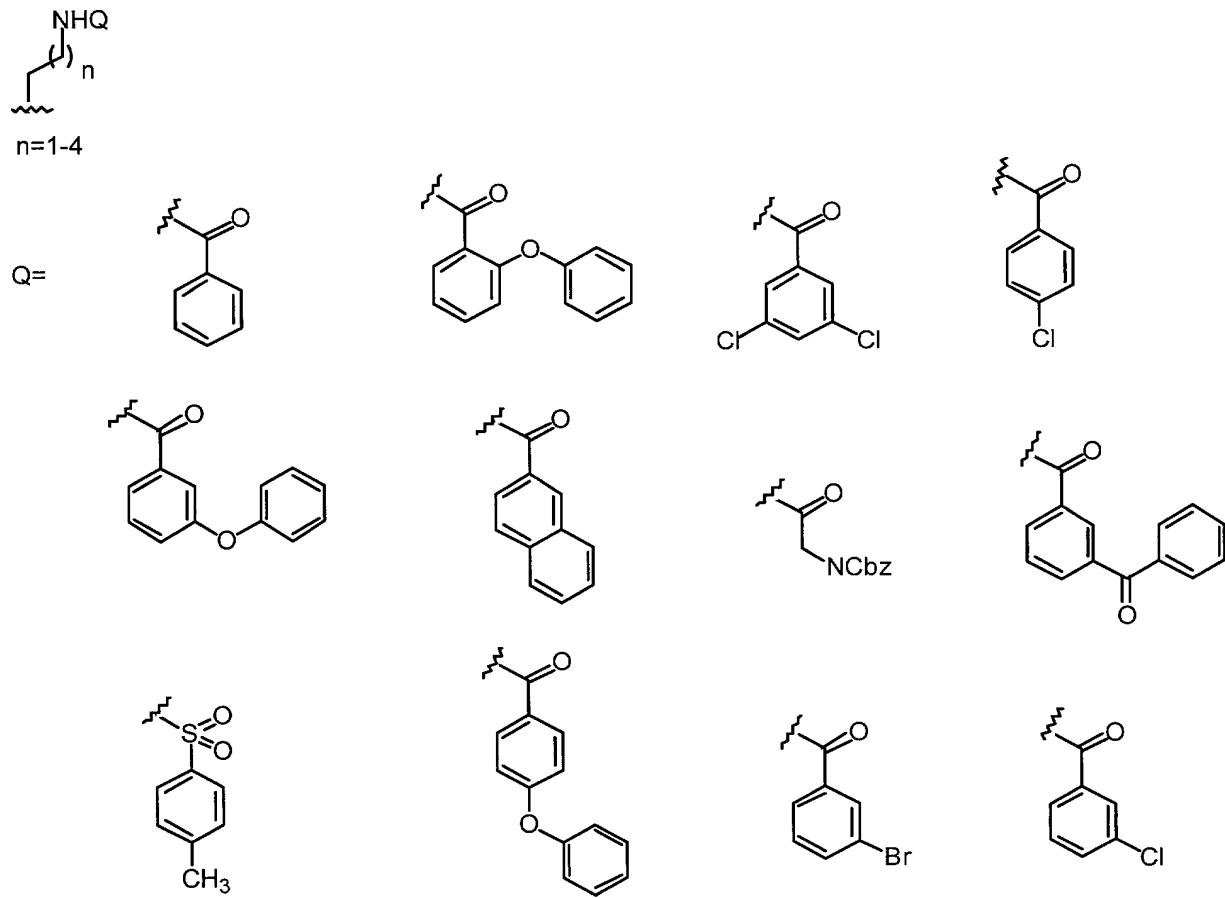
$Y^{18} = F, COOH$,

14. The compound of claim 13, wherein J is selected from the group consisting of:

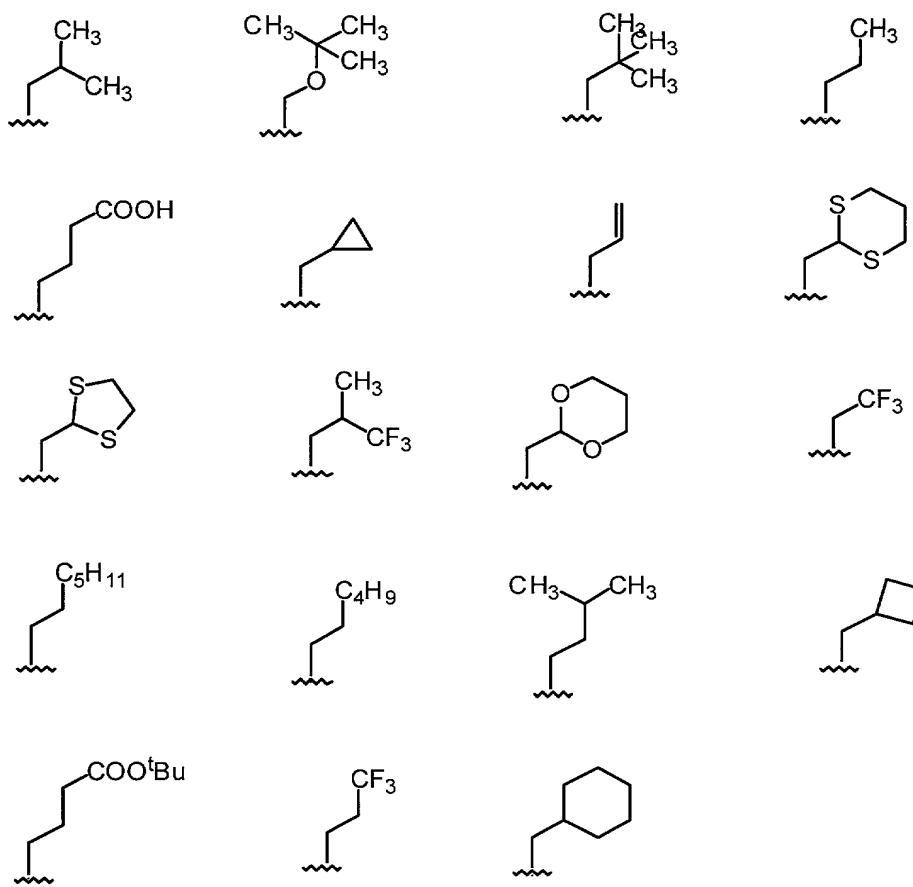


15. The compound of claim 14 where in J is H, CH₃ or Bn.
5 16. The compound of claim 15 wherein G is selected from moieties:



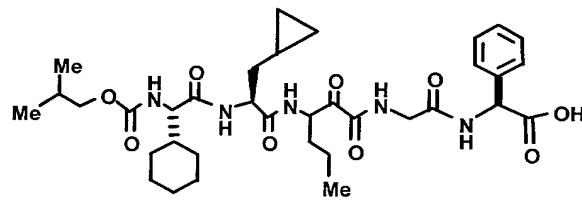
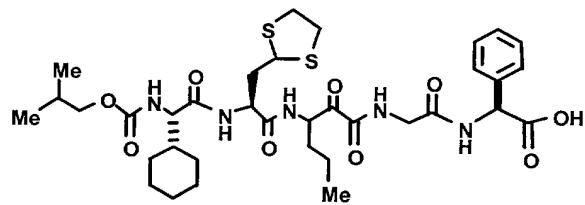
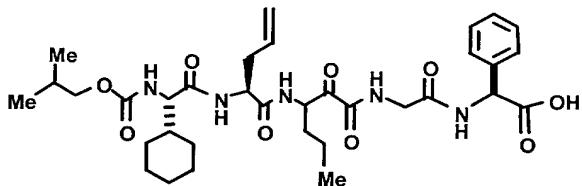
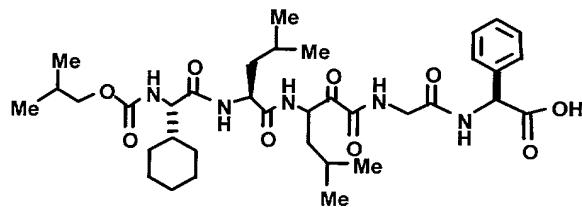


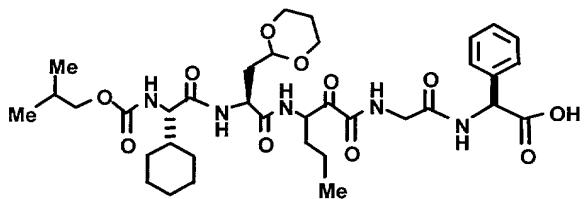
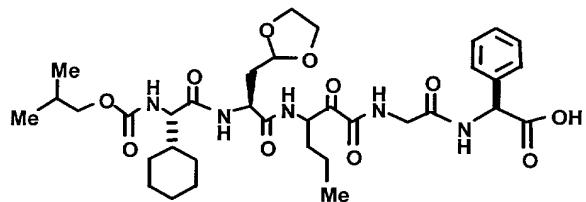
5 17. The compound of claim 16, wherein G is selected from the group consisting of :



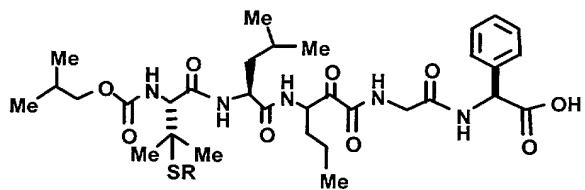
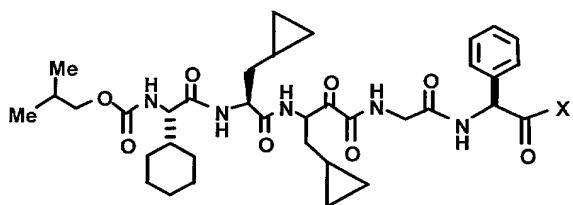
18. A pharmaceutical composition comprising as an active ingredient a compound of claim 1.
19. The pharmaceutical composition of claim 18 for use in treating disorders associated with Hepatitis C virus.
- 5
20. The pharmaceutical composition of claim 18 additionally comprising a pharmaceutically acceptable carrier.
21. A method of treating disorders associated with the HCV protease, said method comprising administering to a patient in need of such treatment a pharmaceutical composition which composition comprises therapeutically effective amounts of a compound of claim 1.
- 10
22. The method of claim 21, wherein said administration is via subcutaneous administration.
23. The use of a compound of claim 1 for the manufacture of a medicament to treat disorders associated with the HCV protease.
- 15

24. A method of preparing a pharmaceutical composition for treating disorders associated with the HCV protease, said method comprising bringing into intimate contact a compound of claim 1 and a pharmaceutically acceptable carrier.
- 5 25. A compound exhibiting HCV protease inhibitory activity, including enantiomers, stereoisomers, rotamers and tautomers of said compound, and pharmaceutically acceptable salts or solvates of said compound, said compound being selected from the group of compounds with structures listed below:





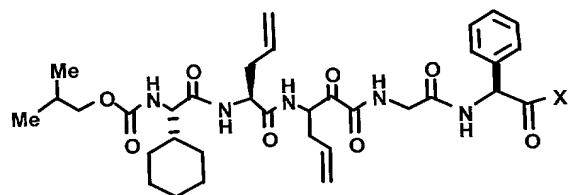
5

 $R = Me$ $R = Benzyl$ 

10

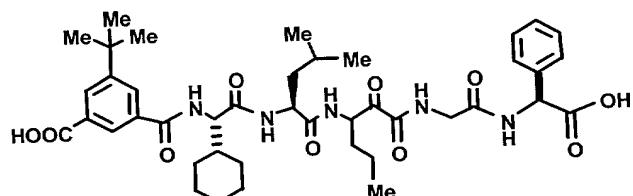
 $X = O^tBu$ $X = OH$ $X = NH_2$ $X = NMeOMe$ $X = NMe_2$

180

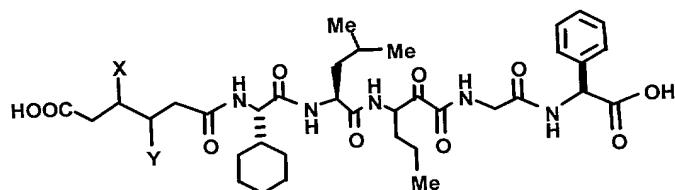


X = O^tBu

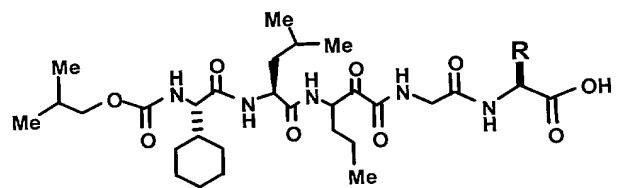
X = OH



5

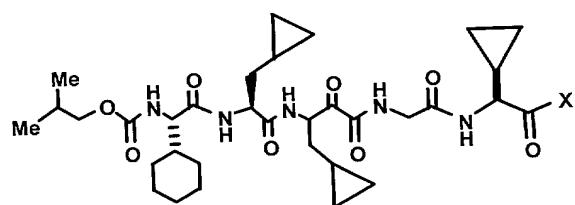


X = H, Y = tBu; X = tBu, Y = H

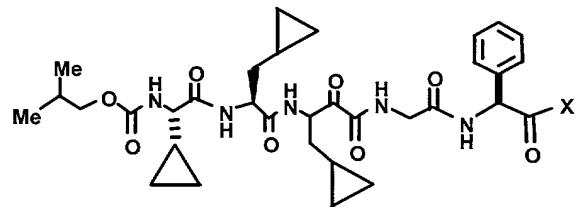
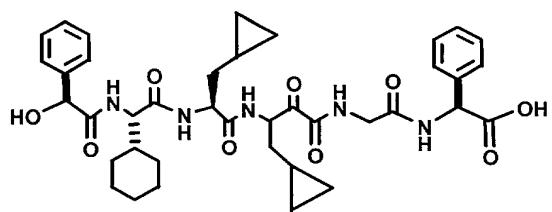


R = Propargyl; R = Allyl

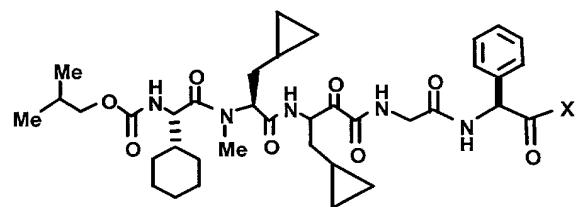
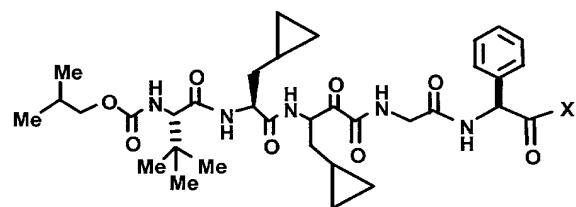
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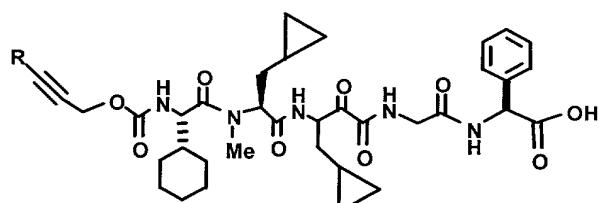
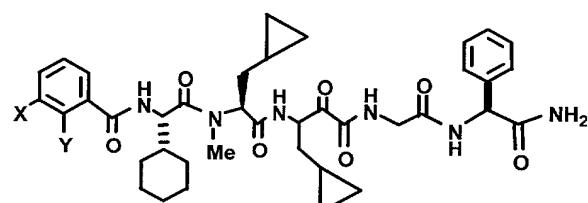
X = O^tBu; X = OH

 $X = \text{O}^{\text{t}}\text{Butyl}$ $X = \text{OH}$

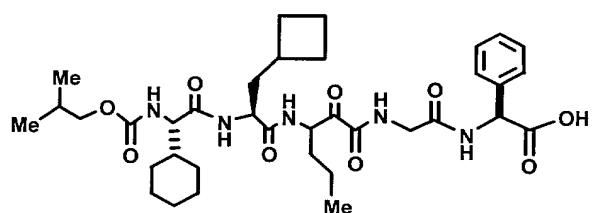
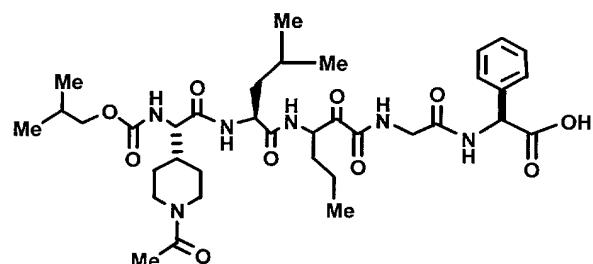
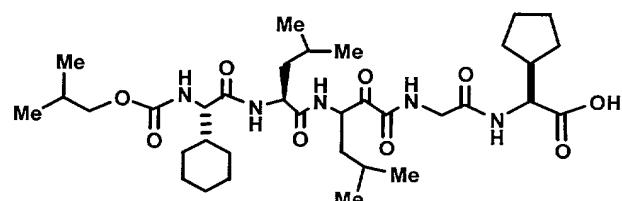
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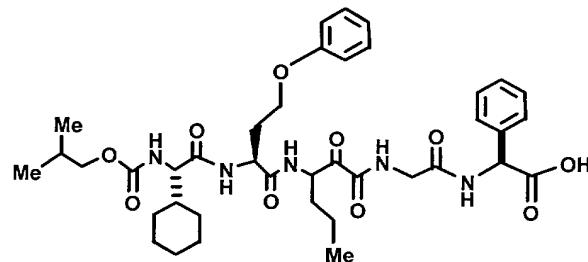
 $X = \text{O}^{\text{t}}\text{Butyl}$ $X = \text{OH}$ $X = \text{NMe}_2$  $X = \text{O}^{\text{t}}\text{Bu}$ $X = \text{OH}$

10

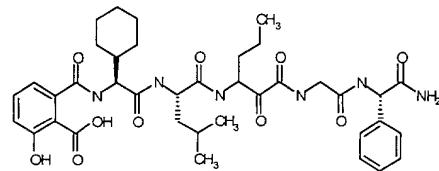
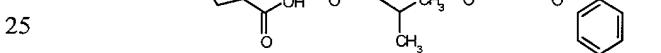
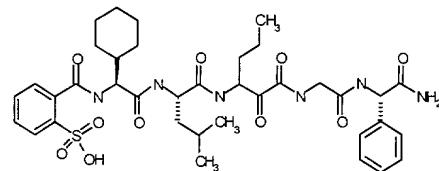
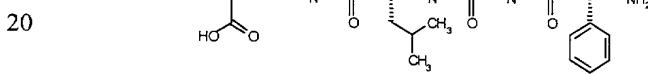
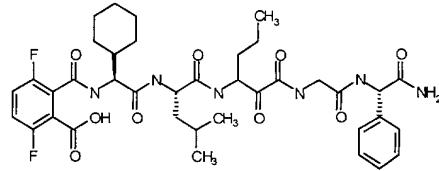
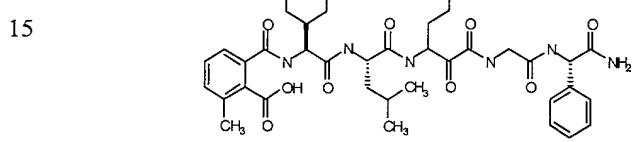
 $R = t\text{Bu}$ $R = \text{H}$ $R = \text{Me}$  $X = \text{H}, Y = \text{COOH}$ $X = \text{COOH}, Y = \text{H}$

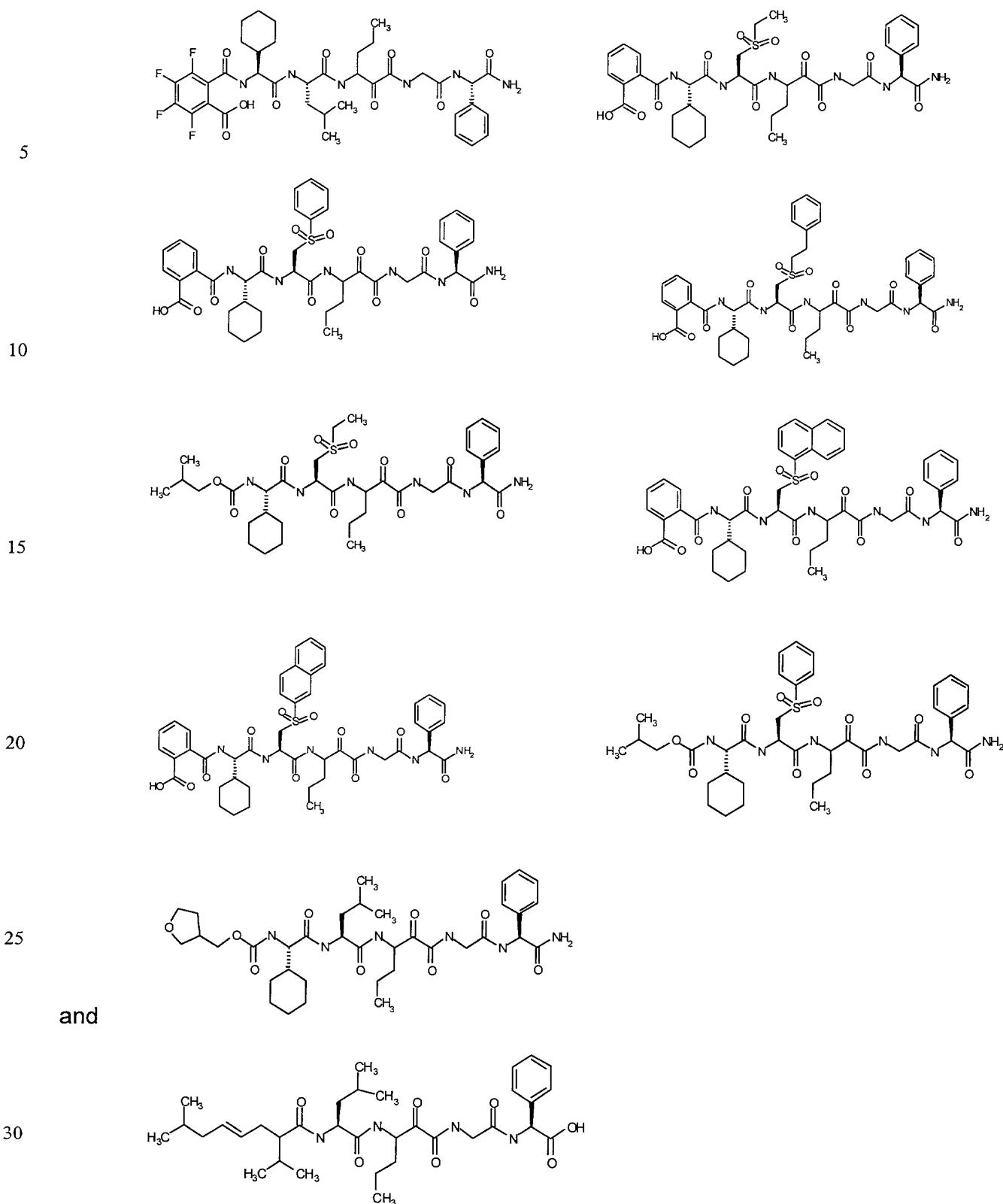
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26. A pharmaceutical composition for treating disorders associated with the HCV protease, said composition comprising therapeutically effective amount of one or more compounds in claim 25 and a pharmaceutically acceptable carrier.
- 5 27. The pharmaceutical composition of claim 26, additionally containing an antiviral agent.
28. The pharmaceutical composition of claim 26 or claim 27, still 10 additionally containing an interferon.
29. The pharmaceutical composition of claim 28, wherein said antiviral agent is ribavirin and said interferon is α -interferon.
30. A compound selected from the group consisting of:





- 1005720-2100660
- or an enantiomer, stereoisomer, rotamer or tautomer thereof, or a pharmaceutically acceptable salt or solvate thereof, wherein the compound exhibits HCV inhibitory activity.
- 5 31. A pharmaceutical composition, comprising one or more compounds of claim 30.
32. A method of treatment of an hepatitis C virus associated disorder, comprising administering an effective amount of one or more compounds of claim 30.
- 10 33. A method of modulating the activity of hepatitis C virus (HCV) protease, comprising contacting HCV protease with one or more compounds of claim 30.
34. A method of treating, preventing, or ameliorating one or more symptoms of hepatitis C, comprising administering an effective amount of one or more compounds of claim 30.
- 15 35. The method of claim 33, wherein the HCV protease is the NS3/NS4a protease.
36. The method of claim 35, wherein the compound or compounds inhibit HCV NS3/NS4a protease.
- 20 37. A method of modulating the processing of hepatitis C virus (HCV) polypeptide, comprising contacting a composition containing the HCV polypeptide under conditions in which the polypeptide is processed with one or more compounds of claim 30.
38. The compound of claim 7, wherein R³ is cyclohexyl.
- 25 39. The compound of claim 11, wherein Y is selected from the group consisting of 2-carboxy-3-hydroxyphenyl, 3-tetrahydrofurylmethoxy, and 2-sulfophenyl.
40. The compound of claim 15, wherein G is selected from the group consisting of ethylsulfonylmethyl, phenylsulfonylmethyl, 2-phenylethylsulfonylmethyl and 1-naphthylsulfonylmethyl.
- 30